PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 13411372	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/000718**	International Filing Date *(day/month/year)* 6 June 2003	Priority Date *(day/month/year)* 7 June 2002
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] C12N 15/02; A61K 67/00		
Applicant ARTHRON LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 5 January 2004	Date of completion of the report 13 September 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **JAMIE TURNER** Telephone No. (02) 6283 2071

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000718

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**7; 11, 12, 18, 20, 37 and 39–41**	**YES**
	Claims	**1–6, 8–10, 13–17, 19, 21–36, 38 and 42**	**NO**
Inventive step (IS)	Claims	**NONE**	**YES**
	Claims	**1–42**	**NO**
Industrial applicability (IA)	Claims	**1–42**	**YES**
	Claims	**NONE**	**NO**

2. Citations and explanations (Rule 70.7)

The applicant's invention resides in the use of the discovery that FcγRIIa transgenic animals are susceptible to autoimmune disease.

Claims 1–12 relate to methods for screening compounds that suppress aberrant immune activity or autoimmune disease, using FcγRIIa transgenic animals.

Claims 13, 21–27 and 42 relate to compounds that can suppress aberrant immune activity or autoimmune disease, when identified by the methods of claims 1–12.

Claims 14–20 relate to methods of treating or preventing autoimmune disease, using the compounds identified by claims 1–12.

Claims 28–41 relate to FcγRIIa transgenic animals.

The following documents identified in the International Search Report have been considered for the purposes of this report.

D1: WO 1995/028959 A1 (SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH) 2 November 1995.
D2: McKenzie SE et al (1999) The Journal of Immunology 162: 4311–4318.
D3: Kwack K et al (1995) Immunology Letters 44: 130–143.
D4: WO 1996/008512 A1 (AUSTIN RESEARCH INSTITUTE AND ANTI-INFLAMMATORY SYNDICATE NO. 1) 21 March 1996.

Novelty (N)

D1discloses transgenic mice expressing human FcRIIa (see, for example, page 44 lines 7 and 32, page 46 line 22 and page 52, line 21), their use in the identification of anti-inflammatory agents (see, for example, the abstract and also page 47, lines 14–25), and the use of these compounds in treatment of inflammation and autoimmune inflammation-related diseases (see, for example, the abstract and also page 51, lines 14–15). As such, this citation is novelty-destroying for claims 1–6, 8–10, 13–17, 21–24, 28, 29, 31, 35, 36, 38 and 42.

D2 discloses transgenic mice expressing human FcγRIIa, whereby the mice show aberrant immune activity (thrombocytopenia) in the presence of anti-CD9 antibodies. This citation is merely one of a large body of published work by the this research group using this transgenic mouse model. Since mice transgenic for human FcγRIIa would inherently have increased susceptibility to autoimmune disease, this citation is novelty-destroying for claims 28–34.

(Continued on supplemental sheet.)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1–4, 6–8, 10–27 and 42 are not fully supported by the description. The applicant's contribution to the art that is disclosed in the description is the use of the discovery that FcγRIIa transgenic animals are susceptible to autoimmune disease. In contrast, claims 1–3 are worded such that. at step (b), the FcγRIIa transgenic animals are assayed for any aberrant immune activity. This aberrant immune activity includes conditions that are completely unrelated to autoimmune disease. The description does not provide an overarching principle whereby FcγRIIa transgenic animals can be used to model any aberrant immune activity. Therefore, in the absence of a restriction of the claims to methods that rely upon the use of FcγRIIa transgenic mice to model autoimmune disease, these claims are not fully supported by the description.

Claims 13–27 and 42 are additionally not fully supported by the description. The description provides support for the use of the discovery that FcγRIIa transgenic animals are susceptible to autoimmune disease. Therefore, the applicant is entitled to claim uses of transgenic FcγRIIa animals in the investigation of autoimmune disease, such as for the identification of agents that suppress autoimmune disease. In contrast, the claims recite the agents identified using such mice. These claims read on the agents *per se*, or uses of these agents, and, since the claims are not restricted to methods of using the discovery of the applicant's invention, namely using FcγRIIa transgenic mice to study autoimmune disease, these claims to the agents alone are beyond the scope that is supported by the description.

Claims 28–41 are not fully supported by the description. As discussed above, the description provides support for the use of the discovery that FcγRIIa transgenic animals are susceptible to autoimmune disease. Therefore, the applicant is entitled to claim uses of transgenic FcγRIIa animals in the investigation of autoimmune disease. In contrast, these claims recite the transgenic FcγRIIa animals themselves, with no reference to their use to study autoimmune diseases. Any transgenic FcγRIIa animals would inherently have the claimed property of susceptibility to autoimmune diseases. The specification does not provide a new principle for the generation of any transgenic FcγRIIa animal. Therefore, in the absence of an inclusion in the claims of features that provide a use for these transgenic animals in the study of autoimmune disease, these claims are not supported by the description.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box I

Rule 67 lists the subject matter which under Article 34(4)(a)(i) an international preliminary examination is not required to be carried out. At item (iv) it specifies methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods, as such matter. However the agreement between WIPO and Australia further qualifies this by excepting from exclusion any subject matter which is examined under national grant procedures. Claims 14–20 have nonetheless been considered because the identified subject matter does not contravene Australian law.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Novelty (N) (continued)

D3 discloses transgenic mice expressing human FcγRIIa (see page 141), whereby the mice show aberrant immune activity (enhanced T cell responses). Since mice transgenic for human FcγRIIa would inherently have increased susceptibility to autoimmune disease, this citation is novelty-destroying for claims 28–34.

D4 discloses earlier work by one of the inventors of the instant application (P M Hogarth). This citation recites methods of testing compounds for their ability to act as Fc receptor antagonists, and pharmaceutical compositions involving these antagonists, including compounds with FcγR-like activity, such as FcRIIa alanine point mutants (Figure 3) and HSA:FcγRII (see figures 9–18, examples, and claims 21 and 52). Also disclosed are anti-FcγRII antibodies. The compositions of the citation are intended for use in the treatment of immune complex diseases, including rheumatoid arthritis (see page 32, lines 20–24). Therefore, these are compounds that reduce aberrant immune activity associated with FcγRIIa, and which could be identified by the methods of claims 1–12. Therefore, since claims 13–17, 19, 21–27 and 42 are directed towards the compounds *per se*, or uses of these compounds, the citation is novelty-destroying for claims 13–17, 19, 21–27 and 42.

Inventive step (IS)

The disclosures of D1–D4 are discussed above.

Claims 7, 11–20, 25–27, 30, 32–34, 37 and 39–41 lack inventive step in the light of D1. The claims differ from the disclosure of D1 in the choice of mouse strain from which the transgenic mice are derived, or in the specific autoimmune inflammatory disease modelled (ie systemic lupus erythematosus, rheumatoid arthritis or collagen-induced arthritis, all immune complex-mediated conditions). Given the direction of D1, in which FcγRIIa transgenic mice are used to model autoimmune inflammatory disease, these additional choices recited by the claims are considered to be technical equivalents of the citation, and thus these claims lack inventive step.

Claims 1, 6, 8, 13, 14, 16, 21 and 23 lack inventive step in the light of either D2 or D3. The claims differ from the disclosures of the citations in the provision of methods for screening compounds that suppress aberrant immune activity, or in the provision of such compounds. Since the citations disclose transgenic mouse models of aberrant immune activity, it is considered a mere workshop improvement over the citation to use such mouse models to identify compounds that suppress this activity, and therefore these claims lack inventive step.

Claims 2–5, 7, 10–12, 15, 17–20, 22, 24–27 and 35–42 are directed towards the use of transgenic mice as models of autoimmune disease. This concept is neither taught nor suggested by D2 or D3, and therefore these claims are considered inventive in light of these citations.

Claims 18 and 20 lack inventive step in the light of D4. These claims are directed towards the use of compounds identified using the applicant's invention, for the treatment of the autoimmune complex disease systemic lupus erythematosus and collagen-induced arthritis. The claims differ from the citation in the choice of autoimmune complex disease. These additional choices recited by the claims are considered to be technical equivalents of the citation, and thus these claims lack inventive step.

Claims 1–12 and 28–42 are directed towards the use of transgenic FcγRIIa mice. Since D4 does not suggest such mice, these claims are considered inventive in the light of D4.

Industrial applicability (IA)

Claims 1–42 meet the requirements of the PCT in regard to industrial applicability.